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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/896,226	BENJAMIN ET AL.	
	Examiner	Art Unit	
	Shaojia A Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *15-22 and 24-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14, 23, and 26-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's response filed on February 27, 2004 wherein claims 35-66 are newly added.

Currently, claims 1-66 are pending in this application.

As indicated in the previous Office Action August 27, 2003, claims 15-22 and 24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected species. Note that the elected specie is the specific compound recited in claim 23. Thus, claim 25 is also drawn to a non-elected species since the active pharmacological agent, raloxifene, tamoxifen, droloxifene, arzoxifene or CP 336156 is not the elected species. Therefore, claims 15-22 and 24-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected species.

Claims 1-14, 23, and 26-66 are examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 55-66 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the particular and specific pharmaceutical agent such as the compound of formula herein, in combination with a filler, disintegrant, wetting agent, and a lubricant or a glidant in specific amounts herein formulated into a pharmaceutical composition herein, does not

reasonably provide enablement for **any** pharmaceutical agents having various and substantially different physical, chemical, and physiological properties, being used with a filler, disintegrant, wetting agent, and a lubricant or a glidant in specific amounts herein formulated into a pharmaceutical composition herein. Note that **any** pharmaceutical agents broadly encompass those known and unknown pharmaceutical compounds with any carriers and excipients as of the instant filing date, as well as those future known compounds.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a pharmaceutical composition for the particular treatment.

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claims are deemed very broad since the claims herein read on **any** pharmaceutical agents having various and substantially different physical, chemical, and physiological properties employed in the composition herein.

The amount of direction or guidance presented:

Functional language at the point of novelty, as herein employed by Applicants, is admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997) at 1406: stating this usage does "little more than outline goal appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". The CAFC further clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added).

In the instant case, the specification merely provides particular compounds formulated into the particular composition.

Thus, Applicants functional language at the points of novelty fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph. Claims employing functional language at the exact point of novelty, such as Applicants', neither provide

those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (*General Electric Company v. Wabash Appliance Corporation et al.* 37 USPQ at 468 (US Supreme Court 1938)).

The predictability or unpredictability: the instant claimed invention is highly *unpredictable* as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art cannot fully described genus, visualize or recognize the identity of the members of the genus, by structure, formula, or chemical name, of the claimed subject matter, as discussed above in *University of California v. Eli Lilly and Co*. Hence, in the absence of fully recognizing the identity of what the active agent is, one of skill in the art would be unable to fully make and use the claimed pharmaceutical system herein.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutic effects, side effects, and especially serious toxicity that may be generated by drug-drug interactions when and/or after administering to a host (e.g., a human) the ***combination*** of any active compounds, which especially broadly encompass those known and unknown compounds having various and substantially different physical, chemical, and physiological properties with any carriers and

excipients as of the instant filing date, as well as those future known compounds, which necessarily require additional or future research to establish or verify their usefulness.

See text book "Goodman & Gilman's The Pharmacological Basis of Therapeutics" regarding possible drug-drug interactions (9th ed, 1996) page 51 in particular. This book teaches that "The frequency of significant beneficial or adverse drug interactions is unknown" (see the bottom of the left column of page 51) and that "Recognition of beneficial effects and recognition of and prevention of adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs that are prescribed" and that "The most important adverse drug-drug interactions occur with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences" (see the right column of page 51) (emphases added). In the instant case, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would not be able to fully predict possible adverse drug-drug interactions occurring with many combinations of any compounds having claimed functional properties in the pharmaceutical compositions herein to be administered to a host. Thus, the teachings of the book clearly support that the instant claimed invention is highly unpredictable.

The presence or absence of working examples and the quantity of experimentation necessary:

As discussed above, only those particular compounds employed in the composition herein is disclosed in the specification. Thus, the evidence in the examples is also not commensurate in scope with the claimed invention and does not

demonstrate criticality of a claimed range of the ingredients in the claimed composition. See MPEP § 716.02(d).

Thus, the specification fails to provide sufficient support of the broad use of any compounds having those functions recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the embodiments of any compounds having those functions recited in the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, the case *University of California v. Eli Lilly and Co.* (CAFC, 1997) and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test all compounds encompassed in the instant claims, with no assurance of success.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 34 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 34 recites the ranges of ingredients, for example "from about 47% to about 77% lactose". There is insufficient antecedent basis for this limitation, the ranges of ingredients, in the claim since the independent claim 32 which claim 34 is dependent from merely recites "lactose from about 32% to about 38%".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-14, 23, and 26-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (5,780,497, or 5,880,137, or EP 0802184 A1, or EP 0802183 A1, PTO-1449 submitted September 28, 2001) in view of Sawicka (Pharmazie 1991, vol.46 page 519-521, PTO-1449 submitted September 28, 2001).

Miller et al. (5,780,497) discloses that the active substituted indole compounds of the general structural formula therein such as the instant elected compound are useful in pharmaceutical compositions containing a pharmaceutically acceptable carrier or excipients to be administered to a mammal. See for example, '497: abstract, col.2 – col.4, and claims 5-7. Miller et al. also teaches broadly a pharmaceutical carrier or excipient system in a pharmaceutical formulation comprising a filler and disintergrant components, a wetting agent, a lubricant, and a glidant including the instant preferred

excipients such as lactose, microcrystalline cellulose, magnesium stearate, and sulfate and Miller et al. teaches that the preparation of the formation comprising the instant compound in various oral forms with these well known excipients is **conventional** to an ordinary skilled artisan in pharmaceutical science (see especially col.7 lines 23-51).

The prior art does not expressly disclose the employment of the specific range of amounts of a filler and disintergrant components, a wetting agent, a lubricant, and a glidant in a pharmaceutical composition herein. The prior art does not expressly disclose the pharmaceutical composition herein further comprising an antioxidant.

Sawicka teaches that adding an antioxidant to a pharmaceutical composition is well known in the art and the stability of a pharmaceutical formulation may be increase by antioxidant addition. See abstract and the entire article.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine the specific range of amounts of a filler and disintergrant components, a wetting agent, a lubricant, and a glidant in a pharmaceutical composition herein, and to further add an antioxidant to a pharmaceutical composition herein.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the specific range of amounts of a filler and disintergrant components, a wetting agent, a lubricant, and a glidant in a pharmaceutical composition herein since it is known that a pharmaceutical composition comprising the instant compound and a pharmaceutical carrier or excipient system in a pharmaceutical formulation comprising a filler and disintergrant components, a wetting agent, a

lubricant, and a glidant based on the prior art. Moreover, the determination and the optimization of amounts of known exicipients such as a known filler, known disintergrant components, a known wetting agent, a known lubricant, and a known glidant in a pharmaceutical composition are considered conventional to an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Further, one having ordinary skill in the art at the time the invention was made would have been motivated to further add an antioxidant to a pharmaceutical composition herein since adding an antioxidant to a pharmaceutical composition is well known in the art.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-14, 23, and 26-66 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5-7 of U.S. Patent No. 5,780,497 in view of Sawicka (Pharmazie 1991, vol.46 page 519-521).

Although the conflicting claims are not identical, they are not patentably distinct from each other for the same reasons as discussed in the 103(a) set forth above.

Claims 1-14, 23, and 26-66 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 5 of U.S. Patent No. 5,880,137 in view of Sawicka for the same reasons as discussed in the 103(a) set forth above.

Thus, the instant claims 1-14, 23, and 26-66 are deemed to be obvious over the 5-7 of U.S. Patent No. 5,780,497 in view of Sawicka, or claim 5 of U.S. Patent No. 5,880,137 in view of Sawicka.

Response to Argument

Applicant's remarks filed February 27, 2004 with respect to this rejection of claims 1-14, 23, and 25-31 made under 35 U.S.C. 103(a) of record in the previous Office Action have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

Applicant's argument that the there is no motivation or suggestion to determine or optimize the specific range of amounts of a filler and disintergrant components, a

wetting agent, a lubricant, and a glidant in the instant claimed composition has been considered but is not found persuasive. As discussed above, the determination and the optimization of amounts of known exicipients such as a known filler, known disintergrant components, a known wetting agent, a known lubricant, and a known glidant in a pharmaceutical composition are considered conventional to an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. The teachings of Miller et al. regarding that making various formulations comprising the instant compound and those well-known excipients is known to be conventional, clearly support the examiner's position in the rejection.

Moreover, Applicant's Examples 1-9 of the specification at pages 27-32 herein have been fully considered but are not deemed persuasive as to the nonobviousness and/or unexpected results of the claimed invention over the prior art. As discussed above, it has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Furthermore, the record contains no unexpected results showing the criticality and significance of the instant claimed ranges of well-known carriers or excipients used in the claimed composition herein. In such a situation, the applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range." In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir.1990). See MPEP § 716.02 - § 716.02(g) for a discussion of criticality and unexpected results. It is noted that arguments of counsel cannot take the

place of factually supported objective evidence. See, e.g., In re Huang, 100 F.3d 135,139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984).

Therefore, the evidence presented in specification herein is not seen to be clear and convincing in support the nonobviousness of the instant claimed invention over the prior art.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is 571.272.0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on 571.272.0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
May 19, 2004